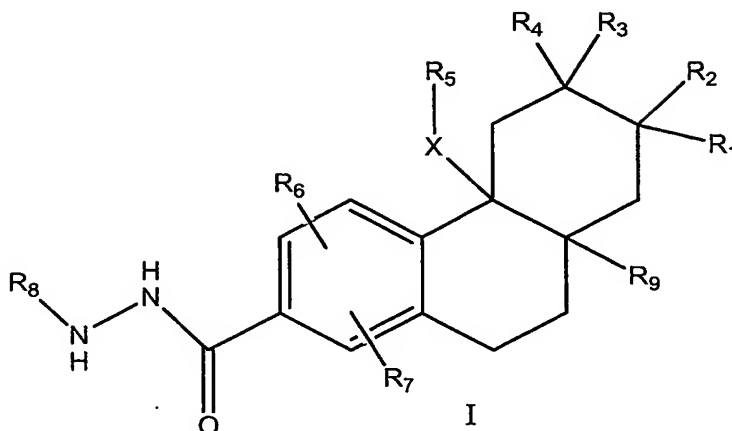


-34-

What is claimed is:

1. A compound of the formula I

5



- an isomer thereof, a prodrug of said compound or isomer, or a
 10 pharmaceutically acceptable salt of said compound, isomer or prodrug;
 wherein R₁ is a) -H, b) -(C₁-C₆)alkyl-A-(C₁-C₆)alkyl, or -(C₁-C₃)alkyl-A-
 (C₁-C₃)alkyl-A-(C₀-C₃)alkyl, wherein A for each occurrence is independently S, O, N,
 OH or NH₂; wherein each carbon atom is optionally substituted with 1 or 2 R_x, c)
 -(C₂-C₁₀)alkenyl optionally substituted with 1 or 2 R_x, d) -(C₂-C₁₀)alkynyl, -ethynyl
 15 (C₁-C₈)alkoxy or -(C₁-C₄)alkoxy(C₁-C₄)alkylethynyl, wherein each carbon atom is
 optionally substituted with 0, 1 or 2 R_x, e) -CH=C=CH₂, f) -CN, g) -(C₃-C₉)cycloalkyl,
 h) -Z-(C₆-C₁₀)aryl, i) -Z-het, j) -C(O)O(C₁-C₆)alkyl, k) -O(C₁-C₆)alkyl, l) -Z-S-R₁₂, m)
 -Z-S(O)-R₁₂, n) -Z-S(O)₂-R₁₂, o) -(C₁-C₈)alkyl, wherein each carbon atom is optionally
 substituted with 1, 2, or 3 halo, p) -NR₁₂O-(C₁-C₆)alkyl or q) -CH₂OR_x;

- 20 Z for each occurrence is independently a) -(C₀-C₆)alkyl, b) -(C₂-C₆)alkenyl or
 c) -(C₂-C₆)alkynyl;

- R_x for each occurrence is independently a) -OH, b) -halo, c) -Z-(C₁-C₈)alkyl,
 wherein each carbon atom is optionally substituted with 1, 2, or 3 halo, d) -CN, e)
 -NR₁₂R₁₃, f) -(C₃-C₆)cycloalkyl, g) -(C₃-C₆)cycloalkenyl, h) -(C₀-C₃)alkyl-(C₆-C₁₀)aryl, i)
 25 -het or j) -N₃;

wherein het is a 5-,6- or 7-membered saturated, partially saturated or
 unsaturated ring containing from one to three heteroatoms independently selected
 from the group consisting of nitrogen, oxygen and sulfur; and including any bicyclic

-35-

group in which any of the above heterocyclic rings is fused to a benzene ring or another heterocycle; and the nitrogen may be in the oxidized state giving the N-oxide form; and optionally substituted with 1, 2 or 3 R_y;

R_y for each occurrence is independently a) -halo, b) -OH, c) -(C₁-C₆)alkyl, d) 5 -(C₂-C₆)alkenyl, e) -(C₂-C₆)alkynyl, f) -O(C₁-C₆)alkyl, g) -O(C₂-C₆)alkenyl, h) -O(C₂-C₆)alkynyl, i) -(C₀-C₆)alkyl-NR₁₂R₁₃, j) -C(O)-NR₁₂R₁₃, k) -Z-SO₂R₁₂, l) -Z-SOR₁₂, m) -Z-SR₁₂, n) -NR₁₂-SO₂R₁₃, o) -NR₁₂-C(O)-R₁₃, p) -NR₁₂-OR₁₃, q) -SO₂-NR₁₂R₁₃, r) -CN, s) -CF₃, t) -C(O)(C₁-C₆)alkyl, u) =O, or v) -Z-SO₂-phenyl;

R₂, R₃ and R₄ are each independently a) -H, b) -halo, c) -OH, d) -(C₁-C₁₀)alkyl, 10 wherein each carbon atom is optionally substituted with 1, 2 or 3 R_x, e) -NR₁₂R₁₃, f) -Z-C(O)O(C₁-C₆)alkyl, g) -Z-C(O)NR₁₂R₁₃, h) (C₁-C₆)alkoxy, i) -Z-O-C(O)-(C₁-C₆)alkyl, j) -Z-O-(C₁-C₃)alkyl-C(O)-NR₁₂R₁₃, k) -Z-O-(C₁-C₃)alkyl-C(O)-O(C₁-C₆)alkyl, l) -O-(C₂-C₆)alkenyl, m) -O-(C₂-C₆)alkynyl, n) -O-Z-het, o) -COOH, p) -C(OH)R₁₂R₁₃ or q) -Z-CN;

15 R₁₂ and R₁₃ for each occurrence are each independently a) -H, b) -(C₁-C₆)alkyl wherein 1 or 2 carbon atoms, other than the connecting carbon atom, may optionally be replaced with 1 or 2 heteroatoms independently selected from S, O and N and wherein each carbon atom is optionally substituted with 1, 2 or 3 halo, c) 20 -(C₂-C₆)alkenyl optionally substituted with 1, 2 or 3 halo or d) -(C₂-C₆)alkynyl wherein 1 carbon atom, other than the connecting carbon atom and the ethynyl atoms, may optionally be replaced with 1 oxygen atom and wherein each carbon atom is optionally substituted with 1, 2 or 3 halo;

or R₁₂ and R₁₃ are taken together with N to which they are attached to form het;

25 X is a) absent, b) -CH₂-, c) -CH(OH)- or d) -C(O)-;

R₅ is a) -H, b) -Z-CF₃, c) -(C₁-C₆)alkyl, d) -(C₂-C₆)alkenyl, e) -(C₂-C₆)alkynyl, f) 30 -(C₆-C₁₀)aryl, g) -CHO, h) -CH=N-OR₁₂, i) -Z-C(O)OR₁₂, j) -Z-C(O)-NR₁₂R₁₃, k) -Z-C(O)-NR₁₂-Z-het, l) -Z-NR₁₂R₁₃, m) -Z-NR₁₂het, n) -Z-het, o) -Z-O-het, p) -Z-(C₆-C₁₀)aryl, q) -Z-O-(C₆-C₁₀)aryl, r) -CHOH-(C₆-C₁₀)aryl or s) -C(O)-(C₆-C₁₀)aryl wherein said (C₆-C₁₀)aryl is optionally substituted with 1 or 2 of the following: -Z-OH, -Z-NR₁₂R₁₃, -Z-NR₁₂het, -C(O)NR₁₂R₁₃, -C(O)O(C₁-C₆)alkyl, -C(O)OH, -C(O)-het, -NR₁₂-C(O)-(C₁-C₆)alkyl, -NR₁₂-C(O)-(C₂-C₆)alkenyl, -NR₁₂-C(O)-(C₂-C₆)alkynyl, -NR₁₂-C(O)-Z-het, -CN, -Z-het, -O-(C₁-C₃)alkyl-C(O)-NR₁₂R₁₃, -O-(C₁-C₃)alkyl-C(O)O(C₁-C₆)alkyl, -NR₁₂-Z-C(O)O(C₁-C₆)alkyl,

-36-

-N(Z-C(O)O(C₁-C₆)alkyl)₂, -NR₁₂-Z-C(O)-NR₁₂R₁₃, -Z-NR₁₂-SO₂-R₁₃, -NR₁₂-SO₂-het, -C(O)H, -Z-NR₁₂-Z-O(C₁-C₆)alkyl, -Z-NR₁₂-Z-NR₁₂R₁₃, -Z-NR₁₂-(C₃-C₆)cycloalkyl, -Z-N(Z-O(C₁-C₆)alkyl)₂, -SO₂R₁₂, -SOR₁₂, -SR₁₂, -SO₂NR₁₂R₁₃, -O-C(O)-(C₁-C₄)alkyl, -O-SO₂-(C₁-C₄)alkyl, -halo or -CF₃;

- 5 R₆ and R₉ are each independently a) -H, b) -halo, c) (C₁-C₆)alkyl substituted with 0 to 3 halo, d) -(C₂-C₆)alkenyl substituted with 0 to 3 halo, e) -(C₂-C₆)alkynyl optionally substituted with 1, 2 or 3 halo, f) -CN, g) -(C₃-C₆)cycloalkyl, h) -(C₃-C₆)cycloalkenyl, i) -OH, j) -O-(C₁-C₆)alkyl, k) -O-(C₁-C₆)alkenyl, l) -O-(C₁-C₆)alkynyl, m) -NR₁₂R₁₃, n) -C(O)OR₁₂ or o) -C(O)NR₁₂R₁₃;
- 10 R₇ is a) -H, b) -(C₁-C₁₀)alkyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃, c) -(C₂-C₁₀)alkenyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃, d) -(C₂-C₁₀)alkynyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃, e) -halo, f) -Z-CN, g) -OH, h) -Z-het, i) -Z-NR₁₂R₁₃,
 15 j) -Z-C(O)-het, k) -Z-C(O)-(C₁-C₆)alkyl, l) -Z-C(O)-NR₁₂R₁₃, m) -Z-C(O)-NR₁₂-Z-CN, n) -Z-C(O)-NR₁₂-Z-het, o) -Z-C(O)-NR₁₂-Z-(C₆-C₁₀)aryl, p) -Z-C(O)-NR₁₂-Z-NR₁₂R₁₃, q) -Z-C(O)-NR₁₂-Z-O(C₁-C₆)alkyl, r) -(C₀-C₆)alkyl-C(O)OH, s) -Z-C(O)O(C₁-C₆)alkyl, t) -Z-O-(C₀-C₆)alkyl-het, u) -Z-O-(C₀-C₆)alkyl-(C₆-C₁₀)aryl, v) -Z-O-(C₁-C₆)alkyl optionally substituted with 1 or 2 R_y, w) -Z-O-(C₁-C₆)alkyl-CH(O), x) -Z-O-(C₁-C₆)alkyl-NR₁₂-het,
 20 y) -Z-O-Z-het-Z-het, z) -Z-O-Z-het-Z-NR₁₂R₁₃, a1) -Z-O-Z-het-C(O)-het, b1) -Z-O-Z-C(O)-het, c1) -Z-O-Z-C(O)-het-het, d1) -Z-O-Z-C(O)-(C₁-C₆)alkyl, e1) -Z-O-Z-C(S)-NR₁₂R₁₃, f1) -Z-O-Z-C(O)-NR₁₂R₁₃, g1) -Z-O-Z-(C₁-C₃)alkyl-C(O)-NR₁₂R₁₃, h1) -Z-O-Z-C(O)-O(C₁-C₆)alkyl, i1) -Z-O-Z-C(O)-OH, j1) -Z-O-Z-C(O)-NR₁₂-O(C₁-C₆)alkyl, k1) -Z-O-Z-C(O)-NR₁₂-OH, l1) -Z-O-Z-C(O)-NR₁₂-Z-NR₁₂R₁₃, m1) -Z-O-Z-C(O)-NR₁₂-Z-het, n1) -Z-O-Z-C(O)-NR₁₂-SO₂-(C₁-C₆)alkyl, o1) -Z-O-Z-C(=NR₁₂)(NR₁₂R₁₃), p1) -Z-O-Z-C(=NOR₁₂)(NR₁₂R₁₃), q1) -Z-NR₁₂-C(O)-O-Z-NR₁₂R₁₃, r1) -Z-S-C(O)-NR₁₂R₁₃, s1) -Z-O-SO₂-(C₁-C₆)alkyl, t1) -Z-O-SO₂-(C₆-C₁₀)aryl, u1) -Z-O-SO₂-NR₁₂R₁₃, v1) -Z-O-SO₂-CF₃, w1) -Z-NR₁₂C(O)OR₁₃ or x1) -Z-NR₁₂C(O)R₁₃;

30 R₈ is het.

2. The compound of claim 1, wherein het in all instances is a heteroaryl having five to seven members.

3. The compound of claim 1, wherein R₁ is a) -H, b) -(C₁-C₁₀)alkyl, wherein each carbon atom is optionally substituted with 1, 2 or 3 R_x, c)

-37-

-(C₂-C₁₀)alkenyl optionally substituted with 1 or 2 R_x, d) -(C₂-C₁₀)alkynyl, wherein each carbon atom is optionally substituted with 1 or 2 R_x, e) -(C₃-C₆)cycloalkyl, f)

-Z-(C₆-C₁₀)aryl, or g) -Z-heteroaryl having five to seven members;

wherein R_x for each occurrence is independently -OH, -halo, and -Z-CF₃;

5 wherein R₂ is a) -H, b) -halo, c) -OH, d) -(C₁-C₆)alkyl optionally substituted with -OH, e) -Z-heteroaryl having five to seven members, f) -COOH, g) -(C₁-C₁₀)alkyl, wherein each carbon atom is optionally substituted with 1, 2 or 3 R_x.

4. The compound of claim 1, wherein R₃ and R₄ are each independently
10 a) -H, b) -halo, c) -OH, d) -(C₁-C₆)alkyl optionally substituted with -OH, e) -Z-heteroaryl having five to seven members, f) -COOH, g) -(C₁-C₁₀)alkyl, wherein each carbon atom is optionally substituted with 1, 2 or 3 R_x;

wherein R_x for each occurrence is independently -OH, -halo, and -Z-CF₃.

5. The compound of claim 1, wherein R₅ is a) -H, b) -Z-CF₃, c) -(C₁-C₆)alkyl, d) -(C₂-C₆)alkenyl, e) -(C₂-C₆)alkynyl, f) -(C₆-C₁₀)aryl, g) -CHO, h)
15 -CH=N-OR₁₂, i) -Z-C(O)OR₁₂, j) -Z-C(O)-NR₁₂R₁₃, k) -Z-C(O)-NR₁₂-Z-heteroaryl having five to seven members, l) -Z-NR₁₂R₁₃, m) -Z-NR₁₂-heteroaryl having five to seven members, n) -Z-heteroaryl having five to seven members, o) -Z-O-heteroaryl having five to seven members.

6. The compound of claim 1, wherein R₆ and R₉ are each independently
20 a) -H, b) -halo, c) (C₁-C₆)alkyl optionally substituted with 1, 2 or 3 halo, d) -(C₂-C₆)alkenyl optionally substituted with 1, 2 or 3 halo, e) -(C₂-C₆)alkynyl optionally substituted with 1, 2 or 3 halo, f) -CN, g) -(C₃-C₆)cycloalkyl, h) -(C₃-C₆)cycloalkenyl, i) -OH, j) -O-(C₁-C₆)alkyl, k) -O-(C₁-C₆)alkenyl, l) -O-(C₁-C₆)alkynyl, m) -NR₁₂R₁₃, n) -C(O)OR₁₂ or o) -C(O)NR₁₂R₁₃.

25 7. The compound of claim 1, wherein R₇ is a) -H, b) -(C₁-C₁₀)alkyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃, c) -(C₂-C₁₀)alkenyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃, d) -(C₂-C₁₀)alkynyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and
30 -N₃, e) -halo, f) -Z-CN, g) -OH, or h) -Z-heteroaryl having five to seven members.

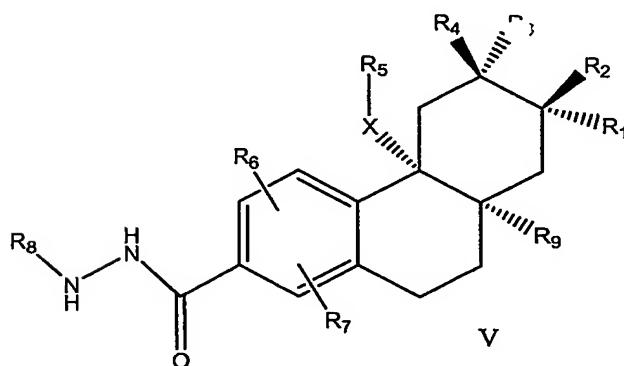
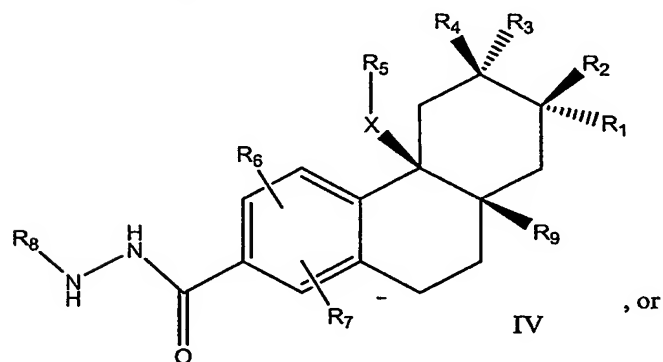
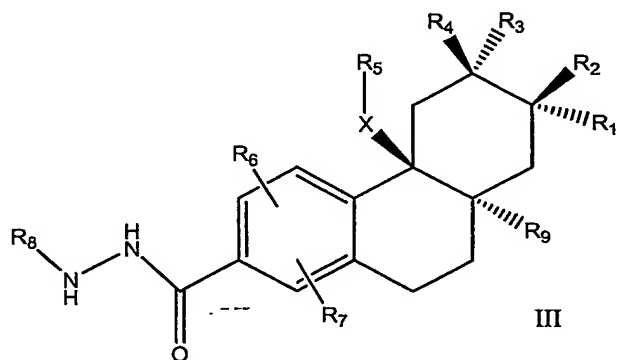
8. The compound of claim 7, wherein R₈ is a 6-membered unsaturated ring.

9. The compound of claim 1 selected from the group consisting of 4b-Ethyl-7-hydroxy-7-trifluoromethyl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-

-38-

carboxylic acid N'-pyridin-2-yl-hydrazide, 4b-Benzyl-7-hydroxy-7-trifluoromethyl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-carboxylic acid N'-pyridin-2-yl-hydrazide, 4b-Ethyl-6,7-dihydroxy-6-methyl-7-thiazol-2-yl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-carboxylic acid N'-pyridin-2-yl-hydrazide

- 5 10. The compound of claim 8, having the formulas III, IV or V:



10

an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug;

wherein R₁ is (C₁-C₁₀)alkyl wherein each carbon atom is optionally substituted with 1, 2 or 3 halo or -Z-heteroaryl having five to seven members;

Z is (C₀-C₆)alkyl;

R₂, R₃ and R₄ are each independently a) -H, b) -halo, c) -OH, d) -(C₁-C₁₀)alkyl, wherein each carbon atom is optionally substituted with 1, 2 or 3 -OH, -halo or -Z-CF₃; wherein R₁ is different from R₂ and R₃ is different from R₄;

5 X is a) absent, or b) -CH₂-;

R₅ is a) -H, b) -Z-CF₃, c) -(C₁-C₆)alkyl, d) -(C₆-C₁₀)aryl or e) -Z-heteroaryl having five to seven members;

R₆ is a) -H, b) -halo, c) (C₁-C₆)alkyl optionally substituted with 1, 2 or 3 halo;

10 R₇ is -H or -(C₁-C₁₀)alkyl optionally substituted with 1, 2 or 3 substituents independently selected from -halo, -OH and -N₃;

R₈ is a 6-membered unsaturated ring containing from one to three heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur;

R₉ is hydrogen.

15 11. The compound of claim 10, wherein R₃ and R₄ are different; wherein said carbon atoms designated C*, independent of each other, has R- or S- configuration.

20 12. The compound of claim 11 selected from the group consisting of all the isomers of the following compounds: 4b-Ethyl-7-hydroxy-7-trifluoromethyl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-carboxylic acid N'-pyridin-2-yl-hydrazide, 4b-Benzyl-7-hydroxy-7-trifluoromethyl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-carboxylic acid N'-pyridin-2-yl-hydrazide, 4b-Ethyl-6,7-dihydroxy-6-methyl-7-thiazol-2-yl-4b,5,6,7,8,8a,9,10-octahydro-phenanthrene-2-carboxylic acid N'-pyridin-2-yl-hydrazide.

25 13. A pharmaceutical composition for treating a disorder selected from the group consisting of inflammatory disorders, endocrine disorders; collagen diseases; dermatologic diseases; allergic states; ophthalmic diseases; respiratory diseases; hematologic disorders; neoplastic diseases; edematous states; and gastrointestinal diseases in a mammal comprising (1) the compound of claims 1 or 10, an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug and (2) at least one pharmaceutically acceptable carrier, vehicle, diluent, excipient.

30 14. A method of treating obesity, diabetes, anxiety, or inflammatory diseases in a mammal comprising administering an effective amount of the

-40-

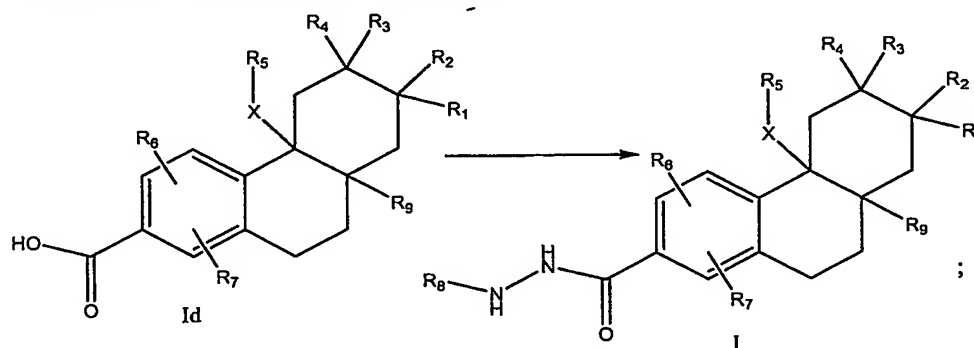
compound of claims 1 or 10, an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug.

15. The method of claim 14, wherein said inflammatory disorders are selected from the group consisting of arthritis, asthma, rhinitis and immunomodulation.

16. A pharmaceutical composition comprising (1) the compound of claim 1, (2) a second pharmaceutically active compound, and (3) at least one pharmaceutically acceptable carrier, vehicle, diluent, excipient.

17. The pharmaceutical composition of claim 16, wherein the second pharmaceutically active compound is selected from the group consisting of β_3 agonist, a thyromimetic agent, an eating behavior modifying agent, a NPY antagonist, an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, a sorbitol dehydrogenase inhibitor, insulin, troglitazone, sulfonylureas, glipazide, glyburide, chlorpropamide, a glucocorticoid receptor agonist, a cholinomimetic drug, an anti-Parkinson's drug, an antianxialytic drug, an antidepressant drug, or an antipsychotic drug.

18. A process of preparing compounds of formula I, an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug, comprising the step of coupling compound of formula Id with a hydrazine under amide forming conditions:



wherein R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉ and X are as defined in claim 1.